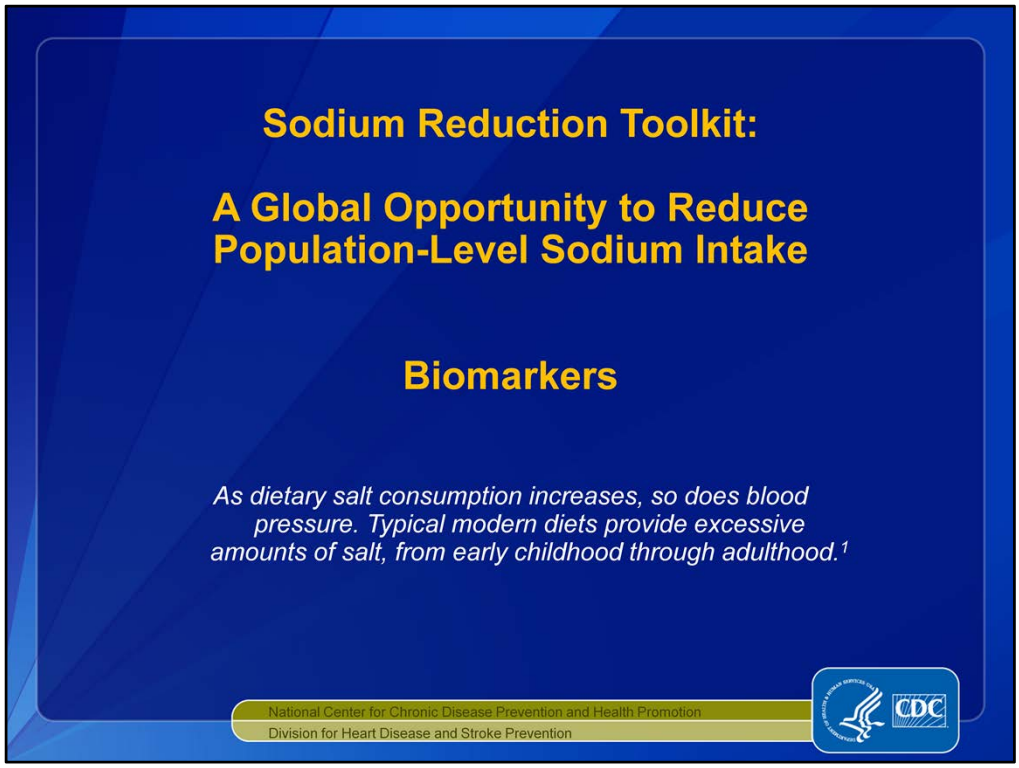
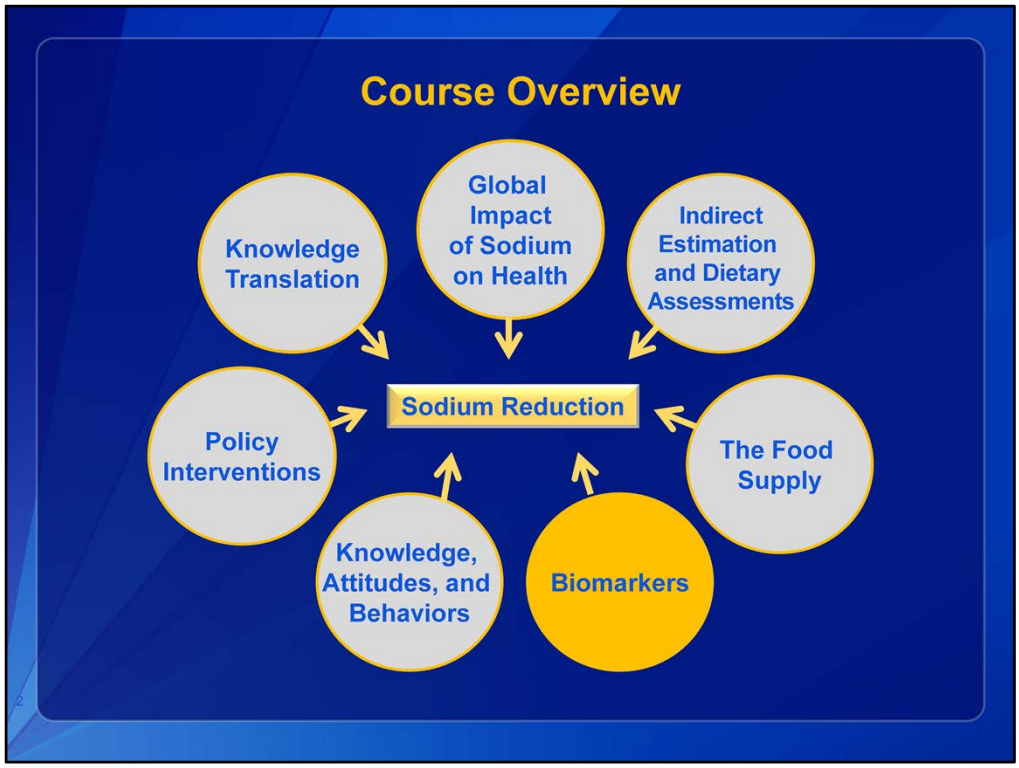


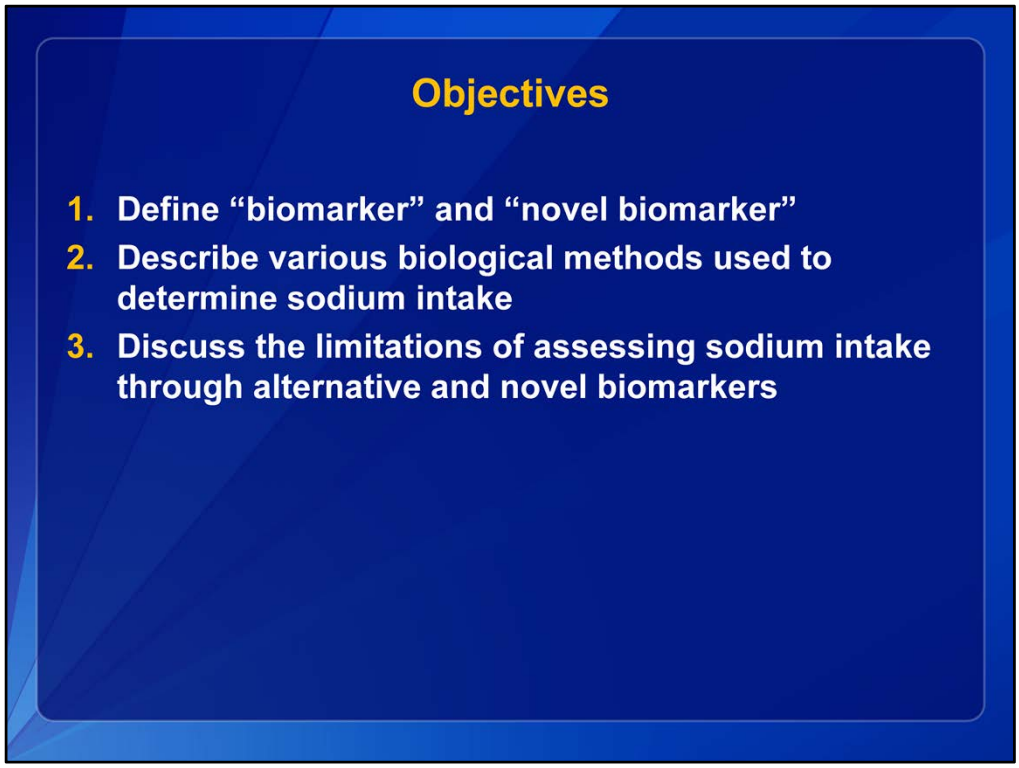
This module is part of the Centers for Disease Control and Prevention's Sodium Reduction Toolkit: A Global Opportunity to Reduce Population-Level Sodium Intake. The toolkit is designed to provide government agencies, international organizations, and other stakeholders with a brief overview, tools, and information necessary to inform strategies to reduce population-level sodium intake.

As dietary salt consumption increases, so does blood pressure. Typical modern diets provide excessive amounts of salt, from early childhood through adulthood.[1]



This module in the Sodium Reduction Toolkit covers methods to evaluate sodium intake through biomarkers. Other modules in the toolkit provide information about the global impact of sodium on health; methods to evaluate sodium intake through indirect estimation and dietary assessments; analysis of sodium in the food supply, including how to create a database to assess sodium in the processed food supply; knowledge, attitudes, and behaviors related to sodium intake and health; strategies for using sodium-reduction policy interventions to reduce sodium intake; and the process of translating and sharing evidence-based research. Each module also includes examples and a list of top 10 resources.

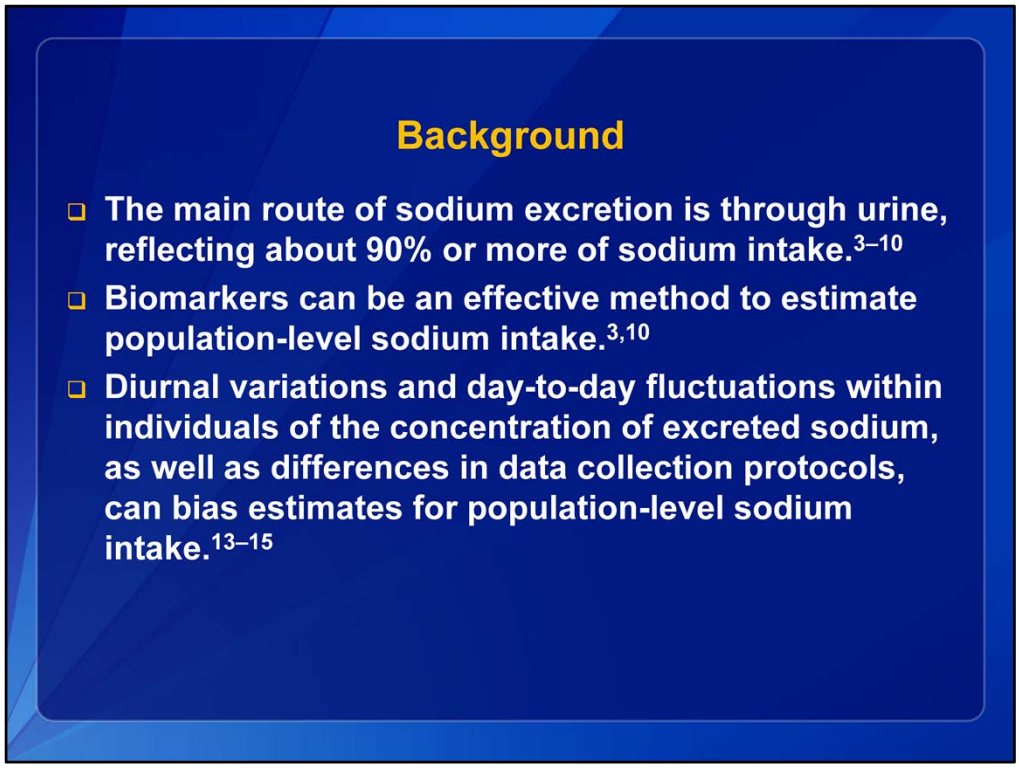
Please note that throughout this module, the term “salt,” also known as sodium chloride, is not synonymous with the term “sodium.” Modules in this series use the term “salt” when referring to sodium chloride and sodium when referring to sodium. A list of conversions for salt and sodium is available on the toolkit web page.



The objectives of the Biomarkers module are to:

1. Define “biomarker” and “novel biomarker.”
2. Describe various biological methods used to determine sodium intake.
3. Discuss the limitations of assessing sodium intake through alternative and novel biomarkers.

Biomarkers are key molecular or cellular events that link a specific exposure to a health outcome. In this case, excess sodium consumption is the specific exposure, and high blood pressure is the health outcome.[2] Examples and considerations are included. Please note that the examples and recommendations provided should be used for training purposes only and do not necessarily imply that they are appropriate for use in your country.



Under normal conditions, the body's main route of sodium excretion is through urine.[3] Studies show that that the average amount of excreted sodium reflects about 90 percent or more of total sodium intake.[4–9] As such, urinary biomarkers can be an effective method to estimate population-level sodium intake.[3,10]

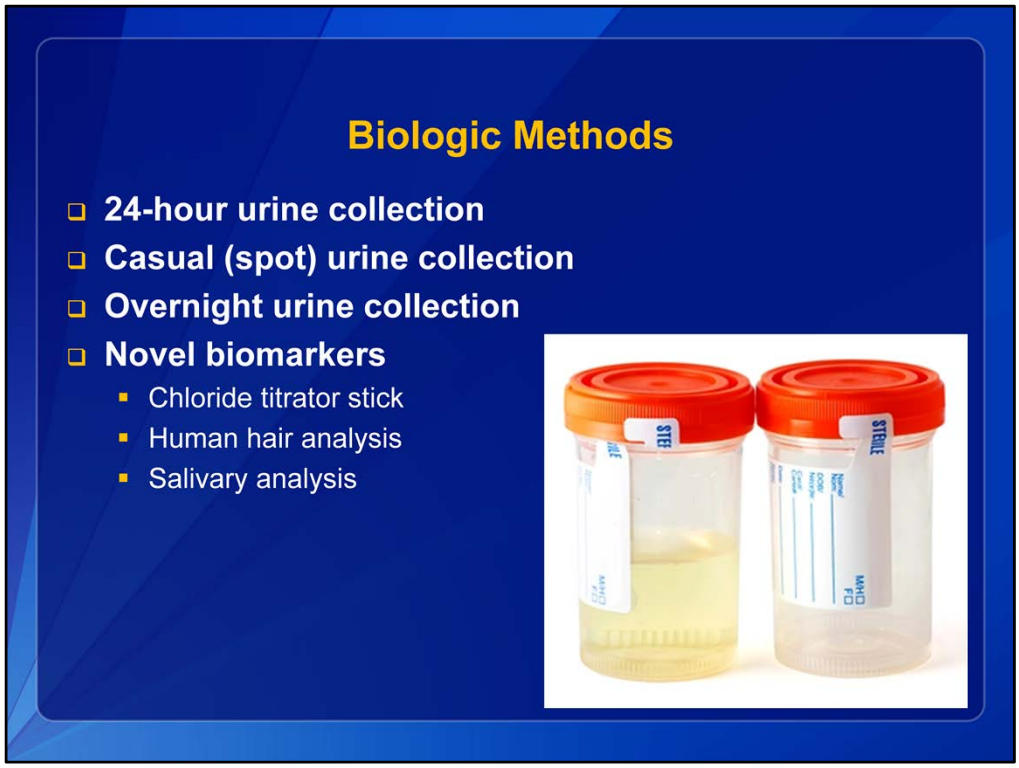
Data obtained through this method can be used to develop, implement, and monitor trends in sodium intake as well as evaluate the effectiveness of sodium reduction policies and initiatives. [3,10] The United Kingdom and New York City's National Salt Reduction Initiative used biomarker methods to estimate the impact of their sodium reduction efforts.[11,12]

Due to individual and diurnal variations in sodium excretion, identifying a method of urine collection that is simple yet accurate has been a challenge.[13–16]
The concentration of sodium in urine can also fluctuate with recent food and beverage intake,[17] physical activity,[18] the environment,[19] and medication use.[20] Some antibiotics and diuretics can produce artificially high test results, and some corticosteroids and nonsteroidal anti-inflammatory drugs can artificially lower test results.[20] These factors must be considered when determining baseline levels and trends for population sodium intake.

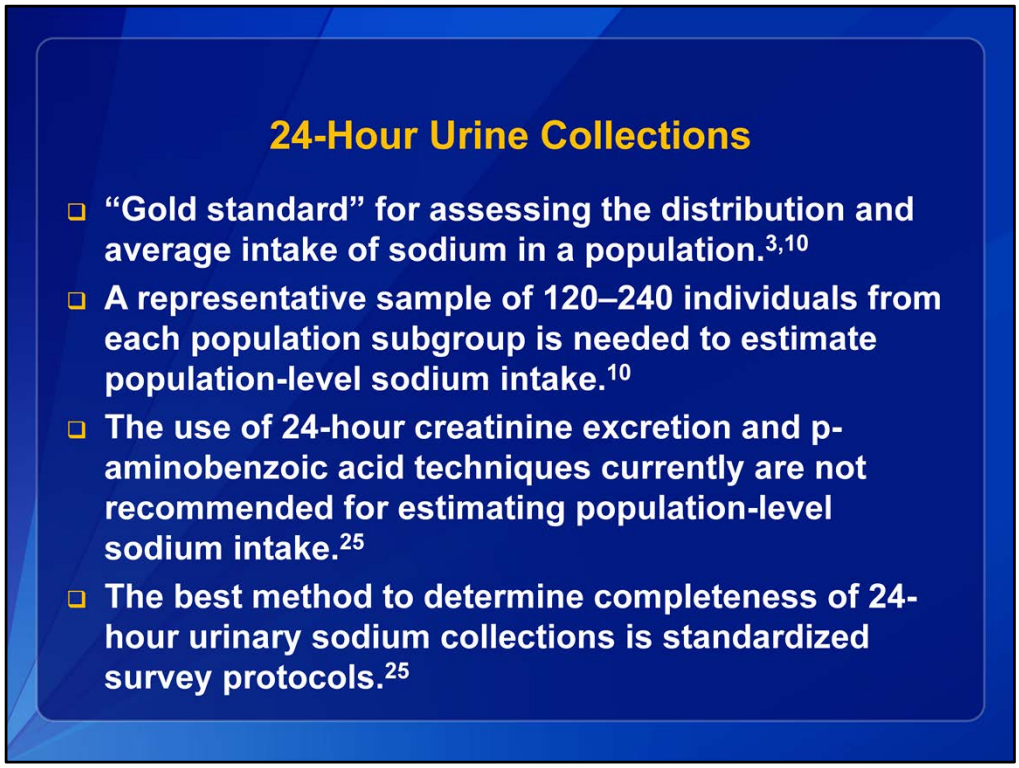
In healthy individuals, diurnal variation in sodium excretion is lower from midnight through the morning and higher during the day and into the evening.[13–16,21] The reverse—higher electrolyte excretions of sodium at night—occurs among individuals with hypertension and African Americans.[21–24] Variation can also occur during the data collection process if incomplete or inaccurate urine samples are accounted for or if the timing of the urine collection is inconsistent.[19,22]

Due to diurnal variations and day-to-day fluctuations within individuals of the concentration of excreted sodium, as well as differences in data collection protocols, estimates for sodium intake may be biased. Despite these limitations, assessing population-level sodium intake through urinary biomarkers can be an effective tool for determining baseline and trend data for sodium consumption in the population.

The following slides describe the various methods used to estimate sodium intake.



Various biologic methods to estimate population-level sodium intake have been examined.[25] These methods include 24-hour urine collections, overnight and spot or casual urine collections, and novel biomarkers.[15,19,26–33] Although each method is presented here, 24-hour urine collection is the only valid and reliable biologic marker currently recommended for estimating population-level sodium intake.[34] Research is still under way to evaluate the potential validity and reliability of other methods for estimating population-level sodium intake.[34]



A 24- hour urine collection measures the average concentration of sodium in urine samples over the course of a 24-hour day.[3,10] This method is considered the "gold standard" for assessing the distribution and average intake of sodium in a representative population.[3,25] Due to diurnal and within-individual variations in sodium excretion, accurately estimating the distribution of and mean population sodium intake requires several 24-hour urine collections.[13–16]

The regional expert group for cardiovascular disease prevention through population-wide dietary salt reduction of the World Health Organization and the Pan American Health Organization developed a Protocol for Population Level Sodium Determination in 24-Hour Urine Samples. According to the protocol, a representative sample of 120 to 240 individuals from each population subgroup is needed to estimate population-level sodium intake.[10] The upper range accounts for the possibility of high rates of attrition and incomplete or invalid collections.[10,25]

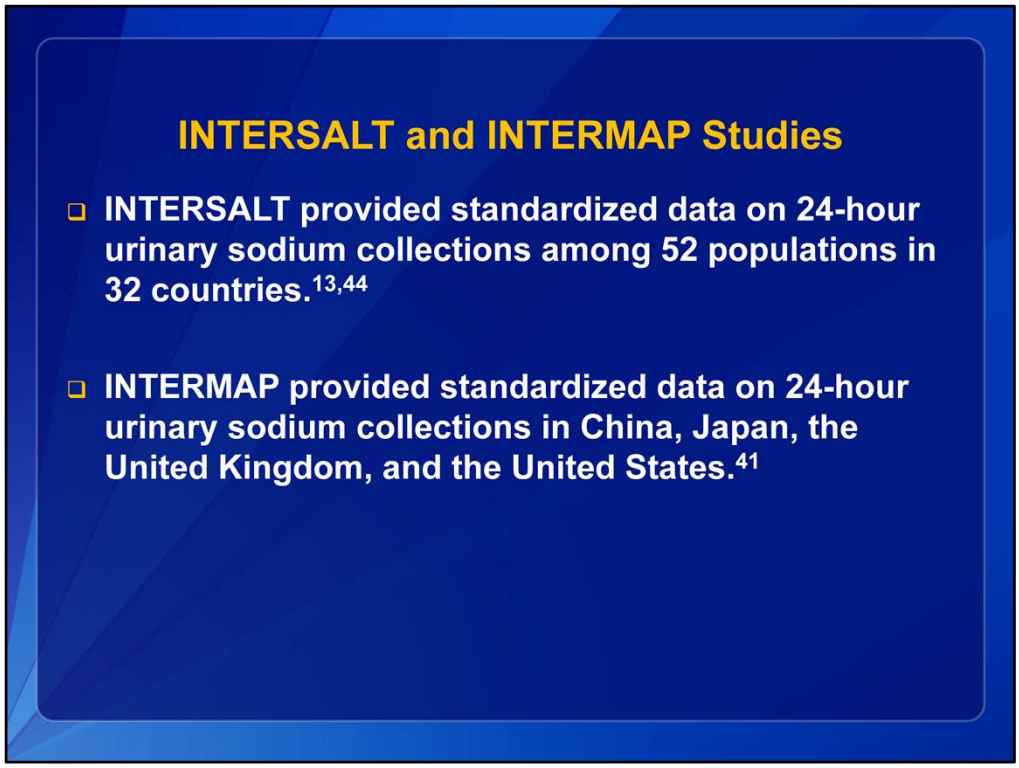
The *p*-aminobenzoic acid technique, casual or spot urine collections, and timed overnight urine collections have been analyzed to estimate 24-hour urinary sodium excretion. To date, these methods have not been validated for use in estimating population-level sodium intake.[9,25,27–29,35–40]

The best available method to determine completeness of 24-hour urinary sodium collections is standardized survey protocols.[25] This method involves training field staff and participants to properly collect, store, and analyze urine samples.[25] Both the INTERSALT Study and the INTERMAP Study used standardized survey protocols.[40,41] If participants reported that "more than a few drops" of urine were lost during the collection, if urine volume was less than 250 milliliters, or if the timing of the collection was not within the range of 20 to 28 hours, participants were asked to repeat the protocol, or a replacement volunteer was used.[40]

Although 24-hour urinary sodium collection is recommended by the World Health Organization[34] and is considered the "gold standard" for assessing population-level sodium intake,[3,25] it has some limitations. The most commonly reported limitations include the high cost to administer and monitor the collections, especially in low- and middle-income countries; difficulty recruiting enough willing volunteers from each population subgroup, which may lead to incomplete urine collections and high rates of attrition; and the overall process associated with this method.[10,25] In one study, only 40 percent of participants provided a complete 24-hour urine collection.[28] Another study reported that 14 separate 24-hour urinary sodium collections per person per subgroup were required to obtain a valid and reliable estimate of sodium intake.[42]

However, other studies have reported success in obtaining valid and reliable 24-hour urinary sodium collections. For example, data from Finland, the United Kingdom, and the INTERSALT study showed that participation rates ranged from 59 percent to 80 percent of volunteers completing 24-hour urine collections.[11,25,43] Some countries with "good" response rates attributed the success to providing clear verbal and written instructions about how to make the urine collection as well as intensive training for field staff. Other countries, such as the United Kingdom, used supermarket or cash voucher incentives to encourage compliance.[11]

The following slides discuss examples from countries that have used 24-hour urinary sodium collections to estimate sodium intake.



The INTERSALT and INTERMAP studies examined the relationship between sodium intake and blood pressure.[13,41,44] Both studies estimated sodium intake by examining data from 24-hour urinary sodium collections.[13,41,44]

In the INTERSALT study, 24-hour urinary sodium collections were obtained from more than 10,000 men and women aged 20 to 59 years from 52 different population groups across 32 countries. This study used the largest set of standardized data on 24-hour urinary sodium samples in the world.[13,44]

The INTERMAP study obtained 24-hour urinary sodium collections from men and women aged 40 to 59 years from 17 population groups in 4 countries: China, Japan, the United Kingdom, and the United States.[41]

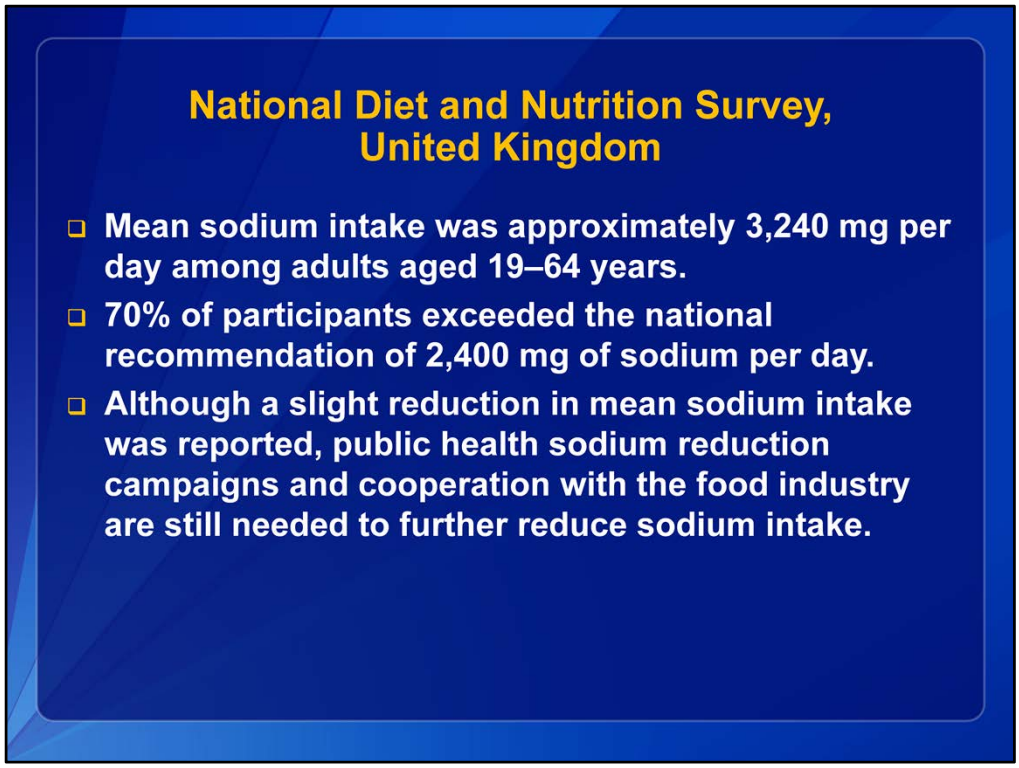
Results of the INTERSALT study showed that across the 52 populations studied, 24-hour urinary sodium excretion was significantly related to median systolic and diastolic blood pressure. Higher blood pressure was associated with older age and the prevalence of hypertension.[13,44]

Most populations had mean 24-hour urinary sodium excretion values ranging from 2,300 milligrams to 5,750 milligrams per day.[13,44] The overall range of 24-hour urinary sodium excretion was as low as 23 milligrams among the Yanomamo Indians of Brazil to as high as 6,000 milligrams in men and 5,300 milligrams in women in Tianjin, China.[13,44] Canada, Columbia, Portugal, the Republic of Korea, and Japan also had values above 4,600 milligrams of sodium per day.[13,44]

It is interesting to note that sodium excretion values in southern parts of China were lower than in the north. This variation is due in part to regional differences in dietary habits, such as intake of sodium and fruits and vegetables.[45]

In addition to 24-hour urine collections, the INTERMAP study also collected blood pressure readings and multiple 24-hour dietary recalls.[41] These recalls were assessed using the multiple pass method. For more information on dietary recalls, please see the Indirect Estimation and Dietary Assessments module.[41]

Except in China, where sodium urine values were higher, the INTERMAP study reported similar findings to that of the INTERSALT study with respect to 24-hour urinary sodium excretions.[41] Results for U.S. adults indicated that median 24-hour urinary sodium excretions were higher than the limits recommended in the *Dietary Guidelines for Americans,* ranging between 2,500 to 3,700 milligrams of sodium per day.[41]

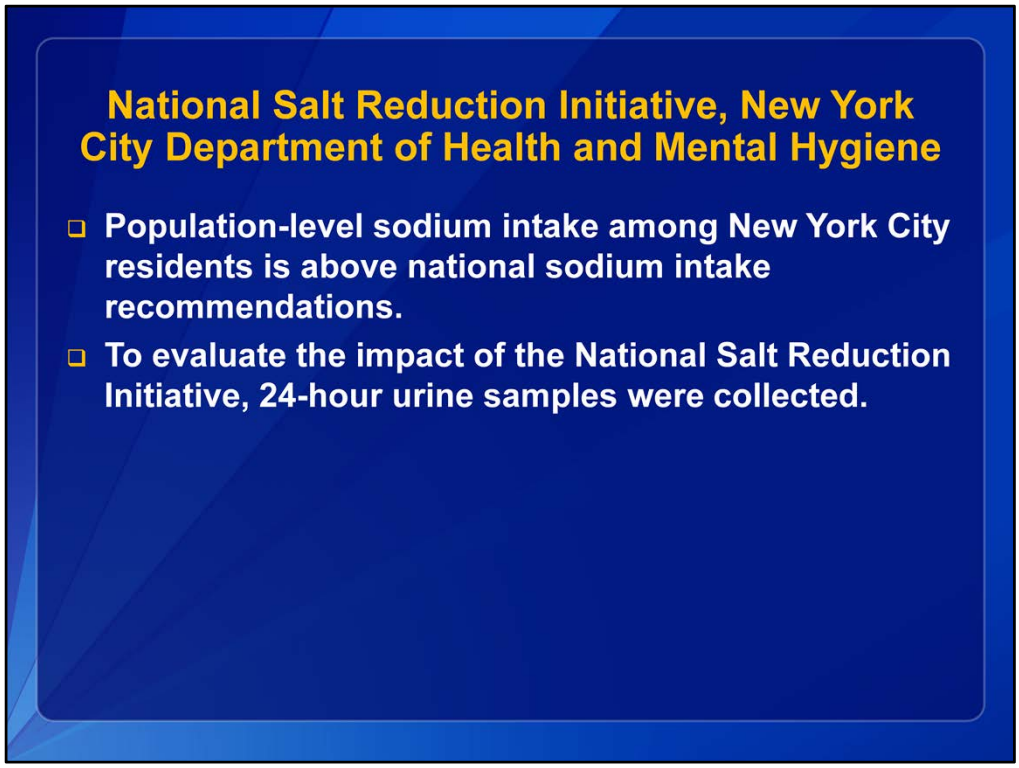


The U.K. Department of Health's Food Standards Agency established a nationwide salt reduction initiative to reduce average daily intake across the population to approximately 2,400 milligrams of sodium, or 6 grams of salt.[11]

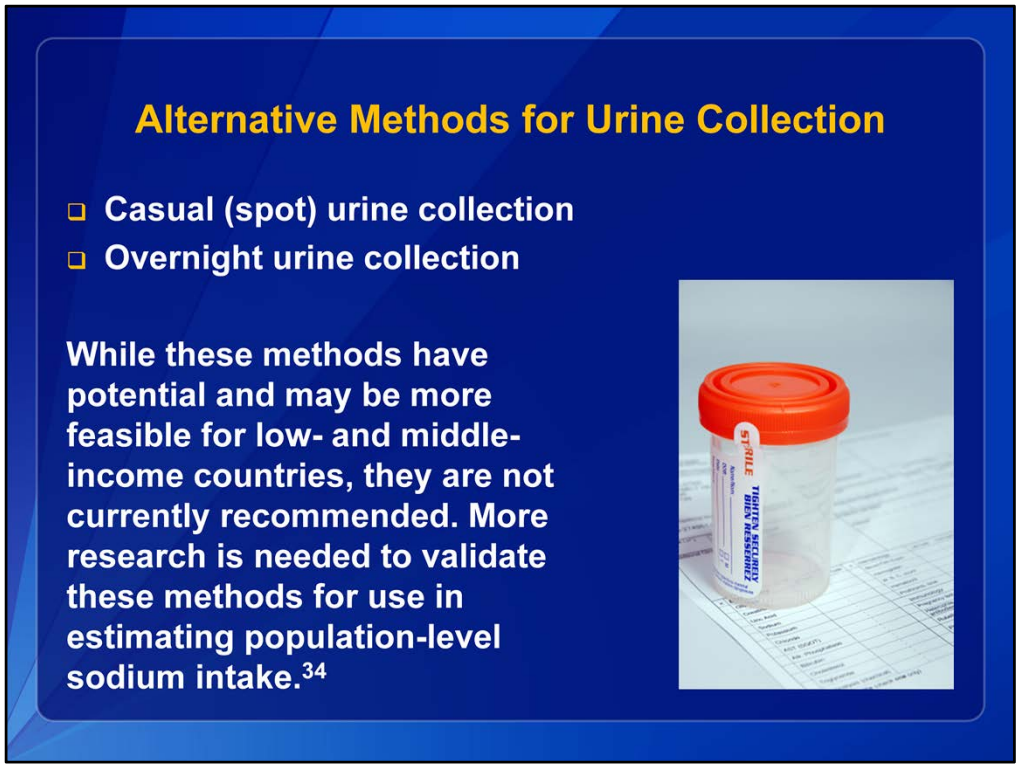
To monitor progress toward meeting the recommendation for sodium intake among the adult population, the Department of Health began collecting urinary sodium excretions from adults in 2000. Twenty-four-hour urine samples were taken from nearly 600 adults aged 19 to 64 years who were enrolled in the National Diet and Nutrition Survey rolling program.

Based on urinary sodium excretion, approximately 70 percent of volunteers were above the national recommendations. The mean estimated daily intake was approximately 8.1 grams of salt, or 3,240 milligrams of sodium.

Although the response rate was 77 percent, the study reported a low number of useable samples in adults aged 19 to 34 years. Although a slight reduction in mean sodium intake was reported, public health sodium reduction campaigns and cooperation with the food industry are still needed to reduce sodium intake in the British population.[11]



The New York City Department of Health and Mental Hygiene leads the National Salt Reduction Initiative, a partnership of more than 85 state and local health authorities and national health organizations aimed to reduce Americans' sodium intake by 20 percent by 2014.[12,46] This voluntary initiative is supported through corporate food manufacturers' and restaurants' commitments to lower sodium in packaged and restaurant food.[12,46] The Centers for Disease Control and Prevention, along with other funders, helped support New York City's evaluation of sodium intake through the use of 24-hour urine collections among 1,800 city residents aged 18 years or older.[12,46] The evaluation is an add-on component to the ongoing New York City Community Health Survey Heart Follow-up Study.



Due to the limitations of using 24-hour urine collections, research has been conducted to find other methods to estimate population-level sodium intake. These include the use of casual or spot urine collections and overnight urine collections.[13,27–29,31–33]

A casual or spot urine collection consists of a single urine sample.[28] A study of 143 healthy American women, aged 30 to 79 years, reported a moderate correlation between 24-hour and spot urine sodium samples.[48] A Scottish study also concluded that estimating mean population-level sodium intake from a single casual urine sample is enough to differentiate between subgroups, similar to a 24-hour urine collection.[49] Results from the 2012 Health Survey for England reported that estimates for sodium intake obtained from using spot urine collections were similar to those of other studies using 24-hour urine collections.[50]

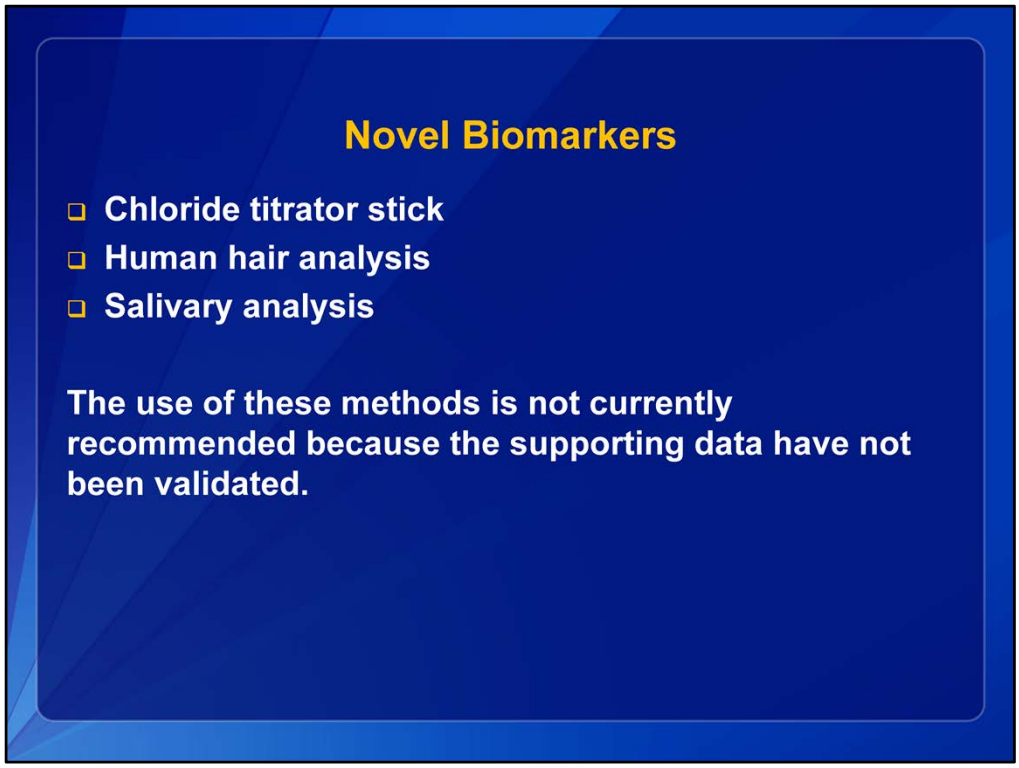
Tanaka and colleagues developed formulas to estimate mean 24-hour urine sodium excretion in casual urine samples.[28] The study concluded that "although this method is not suitable for estimating individual sodium and potassium excretion, these formulas are considered useful for estimating mean population levels of 24-hour sodium and potassium excretion and are available for comparing different populations as well as indicating annual trends of a particular population."[28]

In the INTERSALT study, spot urine collections were positively correlated with 24-hour urine sodium excretions.[51] The results of these studies suggest that despite the limitations of these methods, spot urine samples are possible alternatives to assessing and monitoring baseline levels and time trends in population and subgroup sodium intake.[50]

An overnight urine collection records all urine samples during the night and during the first morning void.[15,25] Before going to bed, participants empty their bladders and discard the urine. After participants have emptied their bladders, the overnight urine collection begins. Participants are instructed to record the time they go to bed and record the time after they provide their first morning void.

Some studies have reported that overnight collections correlated fairly to moderately well with 24-hour urine collections, and burden to the participant was moderate.[22] However, diurnal variation among individuals with high blood pressure and African Americans can bias estimates.[13,22,27–29,31–33]

Although casual or spot urine collections and overnight urine collections may be more feasible for low- and middle-income countries to administer and monitor, research on the use of these methods is still ongoing.[16]

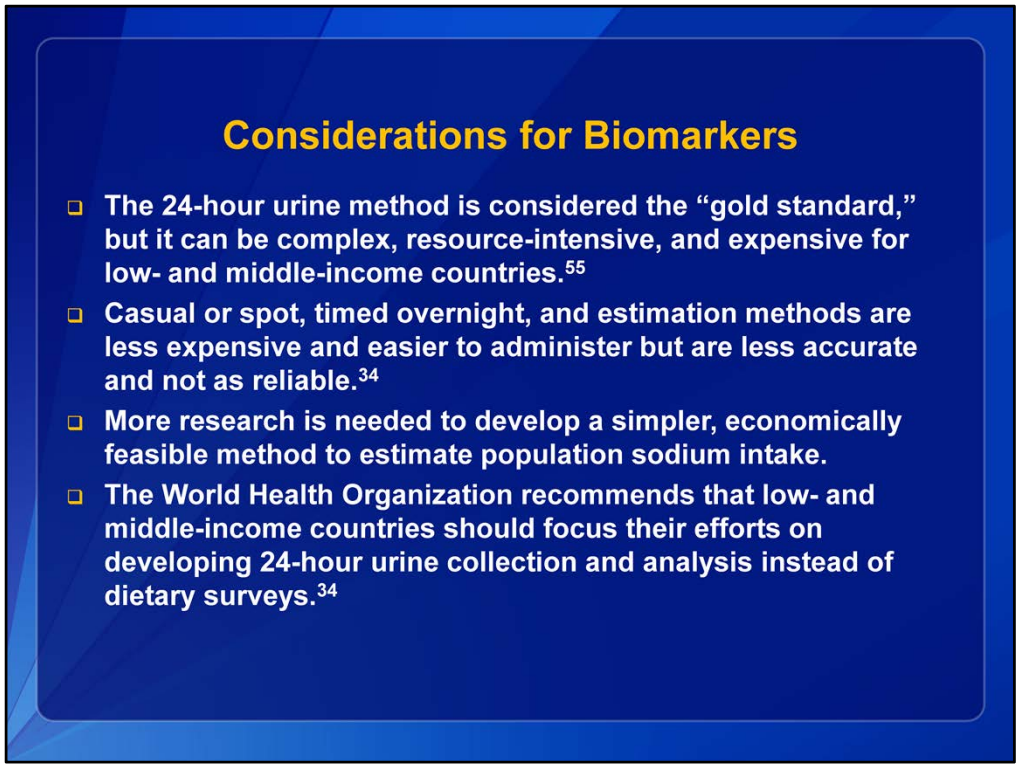


Other techniques to estimate population-level sodium intake have been developed, including a chloride titrator stick and human hair and salivary analysis.[31–33]

To understand why a chloride titrator stick can help estimate sodium intake, it is important to review the characteristics of sodium chloride. Sodium chloride is the chemical name for salt.[52] Salt contains approximately 40 percent sodium and 60 percent chloride.[52] Because the average excretion of sodium reflects about 90 percent or more of sodium intake,[52,53] some studies have tested the practicality of using a chloride titrator stick to estimate population-level sodium intake.[31]

Although estimations for sodium intake using this method have been found to correlate fairly to moderately well with 24-hour and overnight urine collections, this method has not been found to accurately estimate population-level sodium intake.[23,54] Therefore, it is not recommended.

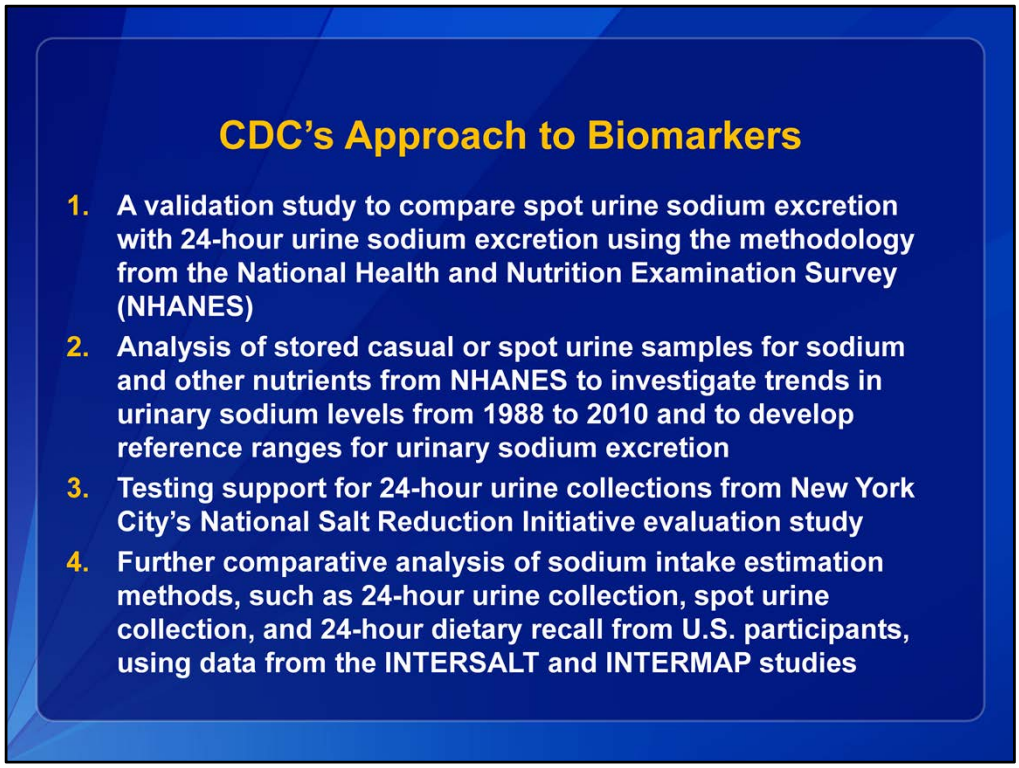
Other studies have analyzed sodium in human hair[32] and in salivary sodium concentrations.[33] Due to external environmental contamination, these methods are not recommended for estimating sodium intake in individuals or populations.



Although the 24-hour urine collection method is considered the "gold standard" for estimating population sodium intake, it can be complex, resource intensive, and expensive, especially for low- and middle-income countries.[55] Although casual or spot, timed overnight, or mathematical equations are less expensive and easier to administer, they have not been validated for use in large-scale studies to estimate population-level sodium intake.[34]

More research is needed to develop a simpler, more economically feasible method to estimate population-level sodium intake.[34,55,56] For now, the World Health Organization recommends that low- and middle-income countries primarily focus their resources on developing a protocol for 24-hour urine collection and analysis.[34] This strategy can help countries determine the most accurate baseline and trend data for sodium intake in the population.

Further, the Institute of Medicine recommends that the Centers for Disease Control and Prevention's Division for Heart Disease and Stroke Prevention conduct additional research on other valid and reliable biomarker methods for estimating population-level sodium intake.[56] Examples of the agency's ongoing efforts to assess biomarkers are discussed next.



The Centers for Disease Control and Prevention has continued to work toward measurement of population sodium intake by assessing various biomarker methods that might be cost-effective and feasible to implement nationwide.

CDC's ongoing work in this area includes the following four projects:

1. A validation study to compare spot urine sodium excretion with 24-hour urine sodium excretion using the methodology from the National Health and Nutrition Examination Survey;
2. Analysis of stored casual or spot urine samples for sodium and other nutrients collected for the National Health and Nutrition Examination Survey, to investigate trends in urinary sodium levels from 1988 to 2010 and to develop reference ranges for urinary sodium excretion;
3. Testing support for 24-hour urine collections from New York City's National Salt Reduction Initiative evaluation study, which CDC co-funds; and
4. Further comparative analysis of sodium intake estimation methods, such as 24-hour urine collection, spot urine collection, and 24-hour dietary recall from U.S. participants, using data from the INTERSALT and INTERMAP studies.

CDC will share results of these efforts as they become available.

The resources included here provide additional background on sodium reduction and biomarkers.

Top 10 Resources

6. Reinivuo H, Valsta LM, Laatikainen T, Tuomilehto J, Pietinen P. Sodium in the Finnish diet: II Trends in dietary sodium intake and comparison between intake and 24-h excretion of sodium. Eur J Clin Nutr. 2006;60:1160–7.
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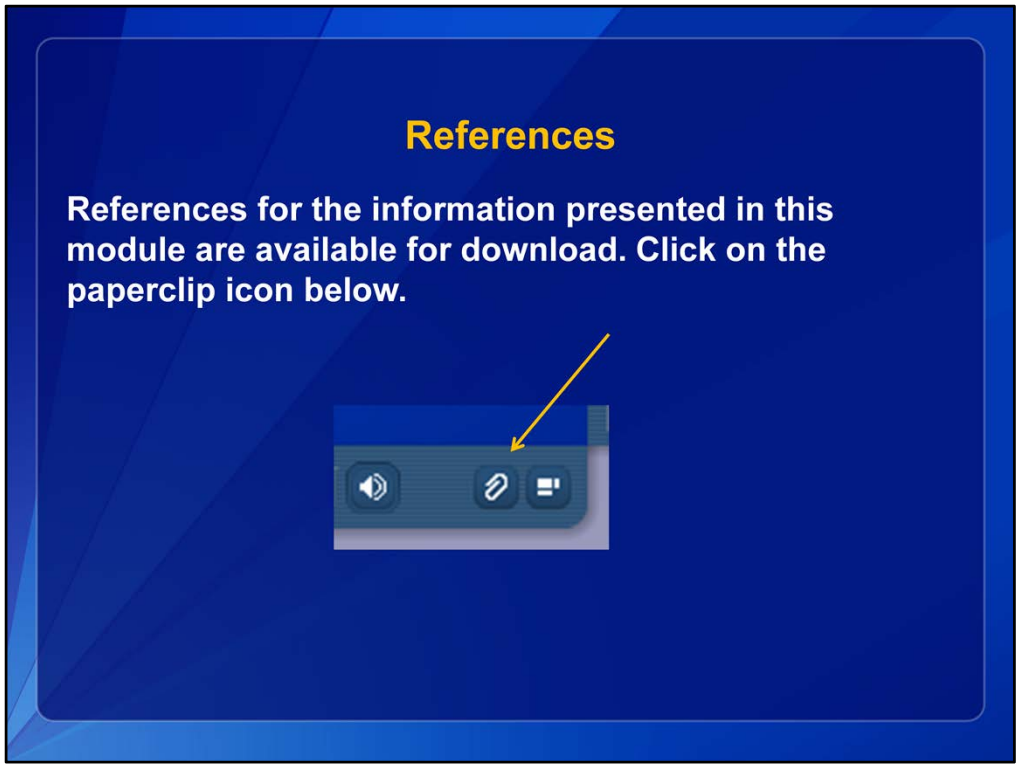
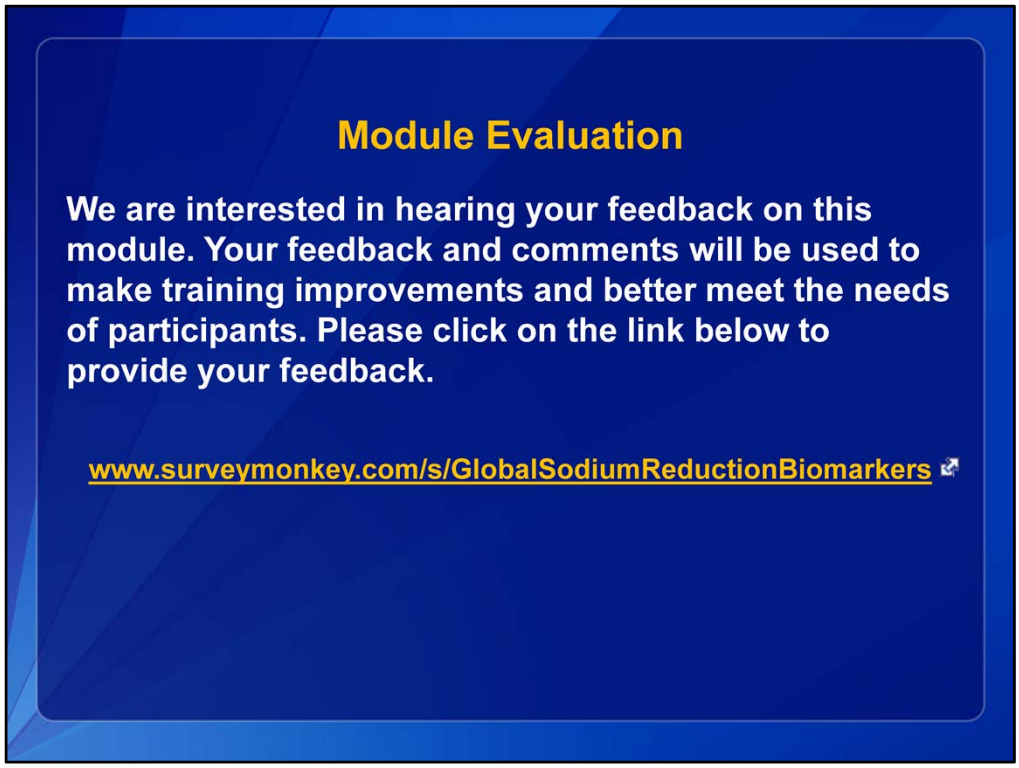


References for the information presented in this module are available for download. Click on the paperclip icon below.



This concludes the Biomarkers module. Please review the other modules to learn more about strategies for reducing sodium intake in your country.

We are interested in hearing your feedback on this module. Your feedback and comments will be used to make training improvements and better meet the needs of participants. Please click on the link below to provide your feedback.

Biomarkers: References

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